IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	Henriksen, et al.
Application No.	:	10/071,505
Filing Date	:	February 8, 2002
Art Unit	:	1617
Title	:	Administering a Gravity Segregation Dispersion by Continuous Infusion
Docket No.	:	NIDN-10439 US

Mail Stop Appeal Brief – Patents
Commissioner for Patents
PO Box 1450
Alexandria VA 22313-1450

APPEAL BRIEF

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I. REAL PARTY IN INTEREST

The real party in interest in this Appeal is Amersham Health AS (now GE Healthcare AS, a part of General Electric "GE").

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences related to the instant appeal.

III. STATUS OF CLAIMS

Claims 1, 3, 5-7, 11-12, and 19 are pending in this application. The Examiner has rejected all of these claims. Claims 1, 3, 5-7, 11-12, and 19 as amended during prosecution are reproduced in the **Claims Appendix** attached hereto. Appellants are appealing the rejections of Claims 1, 3, 5-7, 11-12, and 19.

IV. STATUS OF AMENDMENTS

Appellants filed an Amendment on February 1, 2007 and a final Office Action was mailed on May 3, 2007. No claims were amended subsequent to the Examiner's final rejection that was mailed on May 3, 2007.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent Claim 1 describes a method of administering a gas-containing contrast agent to a subject by continuous infusion, the improvement comprising enhancing product homogeneity by controllably delivering said gas-containing contrast agent from an upper extremity of an essentially vertically positioned syringe and admixing with a flushing medium

prior to administration to the subject, delivering the admixed product to the subject over an infusion period of 5-60 minutes.

Support for claim 1 can be found on page 4, line 28 to page 6, line 30 of the specification.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues for review in this appeal arise from a Final Rejection that was mailed on May 3, 2007. The Examiner rejects claims 1, 3, 5-7, 11-12, and 19 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,033,645 ("Unger").

Therefore, the issue in this appeal is:

1. Whether Unger discloses, teaches, or suggests all the elements of claims 1,3 5-7, 9-11, and 19?

VII. ARGUMENT

The Examiner rejects claims 1, 3, 5-7, 9-11, and 19 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,033,645 ("Unger").

Appellants respectfully request that The Board of Patent Appeals and Interferences ("Board") should reverse the Examiner's rejections for the reasons set forth below.

A. The Examiner's Rejection of Claims 1, 3, 5-7, 9-11, and 19 Should be Reversed Since Unger Fails to Suggest, Disclose, or Teach All the Elements of the Claims

Before discussing the specific differences between the prior art and the present invention, Appellants note that "the prior art itself must provide a motivation or reason for the worker in the art, without the benefit of the Applicant's specification, to make necessary changes in the reference device". See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984).

Furthermore, Appellants respectfully point out here that it is well settled in the law that a reference must be considered not just for what it expressly teaches, but also for what it fairly suggests to one who is unaware of the claimed invention. *In re Baird*, 16 F.3d 380, (Fed. Cir. 1994).

Unlike Unger, a first problem solved by the present invention is to prolong the imaging window when using a gas-containing contrast agent in medical imaging. To solve the problem of the rapid and pronounced, but relatively short lived rise in the backscatter intensity of blood perfused tissues and organs when the gas-containing contrast agent is administered relatively fast, e.g. as a bolus, the contrast agent is administered by continuous infusion. A second problem solved, associated with continuous infusion, is inhomogeneities of gas-containing contrast agent in the apparatus, such as vessels, used for administering the contrast agent. To solve these problems there are several requirements that have to be fulfilled. As is evident from claim 1, these requirements are:

A) controllable delivery from an upper extremity of an essentially vertically positioned syringe;

B) admixing (of the gas containing contrast agent) with a flushing medium prior to administration to the subject;

and

C) delivering the admixed product to the subject over an infusion period of 5-60 minutes.

Appellants respectfully hold that the combination of the requirements A), B) and C) are not suggested, disclosed, or taught by Unger. Furthermore, Unger does not teach all elemental steps of the instant claims. Hence, it is clearly not obvious to one of ordinary skill in the art at the time of Unger to reach the present invention.

Accordingly, the claims of the present invention can not then merely be assumed obvious from the Examiner's subjective view point.

Each of the requirements will now be discussed in more detail below.

Requirement A) - controllable delivery from an upper extremity of an essentiallt vertically positioned syringe.

In Appellants Response dated February 1, 2007 ("Response"), Appellants held that it is impossible to determine from Figure 1 of Unger the position of the syringe 20 and from Figure 2 the position of the syringe (denoted 20' on figure 2), see page 3, paragraphs 1 to 4 of this Response. Furthermore, Appellants held that Unger does not discuss the positioning of the

syringe. In the Office Action dated May 3, 2007 ("Office Action"), the Examiner has never commented on these arguments but merely reiterated that the position of the syringe is vertical with reference to Figure 1. The placement of the syringe is a crucial part of the present invention. The Appellants have surprisingly found that by using a syringe as a delivery reservoir and placing this in a vertical position, with the outlet pointing upwards, the effects of floatation separation is greatly reduced, enhancing the homogeneity of the contrast agent. Appellants therefore maintain this argument as submitted with our Response dated February, 1 2007.

Requirement B) - admixing with a flushing medium prior to administration to the subject.

In Appellants Response, Appellants held that there is no reference whatsoever that can be interpreted to indicate that at least a portion of the contrast agent of Unger is mixed with the flushing agent, let alone that there is no indication in Unger that admixing before administration is intended, see page 3, last paragraph to page 5, paragraphs 1 and 2 of the Response. In the Office Action, the Examiner has not commented on these arguments but merely reiterated that the flushing agent of Unger allows complete transport of the gaseous agent into the bloodstream; thus at least a portion of the contrast agent of Unger is mixed with the flushing agent prior to the administration to the subject. Appellants therefore maintain this argument as submitted with our Response.

Requirement C) - delivering the admixed product to the subject over an infusion period of 5-60 minutes.

In Appellants Response, Appellants held that Unger, col. 64, lines 20-29, which corresponds to claim 209, is not valid prior art under 35 U.S.C 103(a) for the reasons set forth in the Response, namely that the mention of "continuous infusion" or "infusion" is not found in the specification and claims of the corresponding WO 97/48337 published before the priority date of the present application, but first appears in the granted US patent which is published after the priority date of the present application.

The Examiner holds that in order to accept Applicants assertion the Examiner would have to assume that the issued patent, its specification and its claims are not valid and that the Examiner of the issued patent issued an invalid patent. (please see page 2 of the "Office Action"). Appellants respectfully disagree with the Examiner that the argument of an issued invalid patent is relevant in this respect. Appellants have not at all asserted that the US patent is invalid. It is up to a court to decide on the validity of an issued patent, and Appellants have no opinion whatsoever to the validity of the patent in question.

Appellant's argument is that Unger is not a valid 103(a) prior art with regard to the features related to "infusion" in the present invention. In order for a publication to be valid as 103(a) prior art, "the difference between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person skilled in the art to which said subject matter pertains". Appellants also note the factual inquires set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) which is quoted on page 5 of the Office Action.

In the Office Action, the Examiner further cites col. 51, lines 21 to 56 of Unger's patent that at the time when the instant invention was made, the person skilled in the art would have access to WO 97/48337. The person skilled in the art would read p. 75, 1st and 2nd paragraph of WO 97/48337 corresponding to col. 51, lines 21-56 of the US patent as cited by the Examiner. The person skilled in the art would learn that the contrast agent 20' held in the syringe 14' is ejected by pressing the plunger 18' and that the contrast agent will pool or collect in port 44 and also become distributed in the tubing 30'. The flush agent 24' serves to push or drive the contrast agent 20' from its location in the port 44 and/or the tubing 30' into the patient.

As noted above, there is no mention whatsoever in Unger that the contrast agent is to be admixed with the flush agent. The examples of WO 97/48337 provide administration times of the contrast agent. Example 3, 5, 6, 10 and 11 state about 10 seconds, example 4 states about 15 seconds and example 9 states about 50 seconds. None of these administration rates are even close to the infusion period of 5 to 60 minutes as in claim 1 of the present invention. The Examiner should also note that example 2, where the contrast agent is injected during 2 seconds, provides inferior imaging results with severe shadowing. Unger therefore teaches that the time used to push or drive the contrast agent into the blood vessel shall be "controlled", but none of the administration periods that are proposed are even close to the period of 5 – 60 minutes of claim 1 of the present invention. Appellants also note that the function of the flush agent according to Unger is to avoid pooling or accumulation of the contrast agent near the site of injection, see col. 47, line 61 to col. 48, line 10. Appellant would also emphasize that it is a requisite of claim 1 of the present invention that it is the admixed product, i.e. contrast agent and flushing medium, which is delivered over such long period as 5-60

minutes. The Examiner should also note that, unlike the present invention, Unger advices against slow or prolonged injection since this may result in the undesirable dilution of the contrast agent in the bloodstream, see e.g. col. 10, lines 37 to 46 of Unger.

In other words, Unger in effect teaches away from using a slow or prolonged injection since this may result in the undesirable dilution of the contrast agent in the bloodstream, which would discourage a person skilled in the art to do so, see e.g. col. 10, lines 37 to 46 of Unger. 'Teaching away' simply means teaching a solution that would not lead to the claimed subject matter. As noted by the Federal Circuit:

> A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).
>
> *Para-Ordnance Mfg. v. SGS Importers Int'l*, 73 F.3d 1085 (Fed. Cir. 1995).

The teaching of a person skilled in the art does not rely on the words "infusion" and "continuous infusion" but on the the knowledge and recommendations that the person skilled in the art is provided with by "Unger". Accordingly, Appellants maintain that one skilled in the art is not motivated to administer an admixture of the contrast agent and the flush medium over a period of 5 to 60 minutes.

It is important to note here that the Examiner acknowledges that the

specific term "infusion" appeared after our filing date. Thus, the issued '645 patent is not prior art against the present application. Furthermore, Appellants cannot find any basis whatsoever in the Examiner's assertion that the passage quoted from the '645 patent (col. 51, lines 21 to 56) clearly shows that the flush agent does indeed mix with contrast agent prior to ejection into the patient. The Examiner claims that since the flush agent pushes and/or drives the contrast agent forward into the patient, this entails that the flush agent must interact with the contrast agent prior to ejection into the patient. Appellants agrees that to push the contrast medium forward the flush agent will interact with the contrast agent, but it is nowhere mentioned that this "interaction" is any kind of "admixture". Read in conjunction with the references and arguments discussed above, Appellants hold that the person skilled in the art would not read the passage as does the Examiner and assert that the "interaction" is "admixture". Appellants respectfully hold that the Examiner's interpretation here is based on hindsight and should be withdrawn.

The problems of providing improved image quality is noted both by Unger and in the present application. By applying the three requirements of claim 1 listed above in combination, the solution set forth in the claims of the present invention is clearly different from that of Unger and not to mention the fact that Unger teaches away from the present invention as discussed above. Hence, the invention of the claims of the present application is not obvious in view of Unger.

With regards to the alleged lack of showing unexpected results as held by the Examiner on page 8 of the Office Action, Appellants believe that this is not required based on the arguments provided herewith, since the problem is solved in significantly different manners

by Unger and the Appellants. Accordingly, Appellants draw the Examiner's attention to page 5, 5th paragraph to page 6 of the Response, where the results of example 15 are discussed. Please note that the Examiner has not commented on these arguments and explanations in the Office Action.

In view of the aforementioned, Appellants therefore respectfully request that the Board reverse the Examiner's obviousness rejection of claims 1, 3, 5-7, 11-12 and claim 19.

CONCLUSION

In view of the foregoing, Appellants respectfully request that the Board reverse the rejections of Claims 1, 3, 5-7, 11-12, and 19 as set forth in the Office Action mailed May 3, 2007, that the Board allow the pending claims since they are in condition for allowance, and that the Board grant any other relief as it deems proper.

Dated: October 25, 2007

Respectfully submitted,

/Craig M. Bohlken/
Craig M. Bohlken
Reg. No. 52,628
GE Healthcare, Inc.
101 Carnegie Center
Princeton, NJ 08540-6231
Phone No.: (609) 514-6530

VIII. CLAIMS APPENDIX

1. A method of administering a gas-containing contrast agent to a subject by continuous infusion, the improvement comprising enhancing product homogeneity by controllably delivering said gas-containing contrast agent from an upper extremity of an essentially vertically positioned syringe and admixing with a flushing medium prior to administration to the subject, delivering the admixed product to the subject over an infusion period of 5-60 minutes.

2. (canceled)

3. The method of claim 1 wherein delivery of said gas-containing contrast agent from said syringe is controlled by a syringe driver.

4. (canceled)

5. The method of claim 1 wherein said gas comprises sulphur hexafluoride or a perfluorinated low molecular weight hydrocarbon.

6. The method of claim 5 wherein said perfluorinated hydrocarbon is perfluoropropane or perfluorobutane.

7. The method of claim 1 wherein said gas is present as albumin-stabilised microbubbles.

8. – 10. (canceled)

11. The method of claim 1 wherein said flushing medium is normal saline.

12. The method of claim 1 wherein the admixed gas-containing contrast agent and flushing medium are administered by injection.

13.-18. (canceled)

19. The method of claim 1 wherein the flushing medium is administered at a flow rate of 0.5-5 ml/minute.

IX. EVIDENCE APPENDIX

Appellants hereby list the following patent that the Examiner cites against the present invention:

U.S. Patent No. 6,033,645 ("Unger").

This is the evidence relied upon by the Examiner for rejection of appealed Claims 1, 3, 5-7, 11-12, and 19 in the Office Action dated May 3, 2007.

X. RELATED PROCEEDINGS APPENDIX

There are no other appeals or interferences related to the instant appeal.